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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,174	10/12/2000	Hilary Koprowski	JEFF-KOPO1.P	2234

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/673,174	KOPROWSKI ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 17-28* is/are pending in the application.

4a) Of the above claim(s) *17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 20, 2003 has been entered. Claims 1-4 and 17-28 are pending. Claims 17-28 are withdrawn from consideration for the reasons set forth below.

Election/Restrictions

2. Newly submitted claims 17-28 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

New claims 17-28 constitute three groups of invention.

- Claims 17-23 are drawn to a method of producing a full length antibody in a host plant, comprising infecting a plant with two viral vectors.
- Claims 24-27 are drawn to a method of producing a full length antibody in a host plant, comprising infecting a plant with a single vector.
- Claim 28 is drawn to a method of producing a full length antibody in a host plant, comprising infecting a plant with a three vectors.

These three claim sets are drawn to different inventions. The methods require different steps and reagents, and are not disclosed as capable of use together. Each method requires a separate search which is burdensome. Since applicant has received an action on the merits for

the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 17-28 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

3. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donson *et al* (5,316,931) in view of Ma *et al* (*Eur. J. Immunol.* 1994) and Scholthof *et al* (*Annual Rev. of Phytopathol.* 34:299-323, 1996). The Donson and Ma references are previously of record. The claims as amended are drawn to a method for producing a full-length antibody in a host plant using two viral vectors. The viral vectors are each comprised of a movement protein, a coat protein, and a nucleic acid sequence that encodes either a heavy or light chain of an antibody. The vectors are introduced into one host plant, the light and heavy chains are expressed, and a full length antibody is assembled. The full-length antibody can be a monoclonal antibody. The antibody can be directed to a variety of antigens. The host plant is either a dicotyledon or a monocotyledon.

To summarize from previous Office actions, Donson teaches the use of viral vectors to infect plants and express foreign genes. Donson uses recombinant plant viral nucleic acid comprising a viral coat protein coding sequence and a non-native nucleic acid sequence to be transcribed or expressed in the infected host plant. The recombinant plant viral nucleic acids are stable and capable of systemic infection and expression of the foreign protein (abstract). Donson teaches the use of tobacco mosaic virus, TMV (col. 9,lines 14-16). TMV inherently contains a

movement protein, evidenced by Donson *et al* (*PNAS USA*, 88:7204-7208, 1991), previously of record, page 7204, columns 1-2. The movement protein would be expected to be present in Donson's TMV vector absent any indications that it was excluded from the vector. Donson also teaches that antibodies can be produced using the viral vector method (col. 14, lines 59-67) without specifying the method to accomplish antibody production and assembly.

However, Ma teaches the production and assembly of full-length antibodies using a transgenic approach. Genes encoding heavy and light chains are expressed in tobacco plants (dicotyledon) and then crossed, resulting in a full-length assembled antibody (abstract).

It would have been obvious to incorporate the teachings of Ma into Donson's method, by producing heavy and light chains in separate viral vectors, introducing the vectors into one plant, resulting in the an assembled, full-length antibody. One would have been motivated to use produce the light chain and the heavy chain separately (as in Ma) because antibodies are complex proteins consisting of several heteromeric chains. One would have been motivated to use viral vectors instead of a transgenic approach because Scholthof *et al* (*Annual Rev. of Phytopathol.* 34:299-323, 1996) discloses advantages of plant virus gene vectors for transient expression of foreign proteins in plants, versus transgenic gene expression (abstract). Some of the advantages of using autonomously replicating viruses are increased speed and flexibility during early phases of experimentation, high levels of multiplication and high levels of transient gene expression (page 301, first and second paragraphs). One would have had a reasonable expectation of success that separate viral vectors encoding light and heavy chains would assemble into a full length antibody in one plant because Donson teaches successful production

of antibodies using a viral vector in one plant, and Ma teaches a successful method of assembling antibodies.

Applicant's arguments pertaining to the originally presented invention have been carefully considered, but fail to persuade. Applicant's substantive arguments are primarily directed to the assertion that Donson '931 and Donson PNAS disclose only the use of a single recombinant vector, and do not suggest that multiple recombinant viral vectors can be used to express antibody sequences in plants. Applicant states that "one of ordinary skill in the art would not believe that multiple recombinant vectors could or should be used to deliver foreign genes to plant cells simply because single recombinant vectors have been used similarly in the past. One skilled in the art would also not assume that multiple viral vectors would necessarily cause systemic infection of a host plant", page 9 of Applicant's response filed November 20, 2003. Applicant goes on to discuss the concepts of cross protection, limited spread of the virus, stunting of plant growth due to viral infection and stress on the cell as a result of introducing exogenous, self-replicating DNA. Applicant asserts that one skilled in the art at the time of invention would not have been motivated to use multiple vectors given the possible consequences listed above.

In response, the concept of cross-protection relates to viruses/antigens rendering plants resistant to closely related viruses/antigens. The instant claims broadly encompass a first and second viral vector using same virus vector. The concept of limited spread of the viral vector within the plant due to the production of chemotactic factors, viral-binding lectins or pathogenesis related proteins is a problem that can be overcome, as evidenced by Donson '931, which teaches that a plant viral vector can cause systemic infection in a plant (abstract). The

concept of stunted growth is not relevant to the asserted lack of motivation in the references because the claims are not limited to the size of the plant that produces the antibody. The concept of cell stress caused by introducing foreign DNA is also irrelevant to the asserted lack of motivation. Applicant has not shown how cell stress would dissuade one from introducing foreign DNA into a plant. Given the teachings of Donson '931, one would know that introducing a viral vector would result in expression of a desired protein despite any cell stress resulting from the viral vector.

Conclusion

4. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 872-9306. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (571) 272-0896. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (571) 272-0902. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC
Stacy B. Chen
February 18, 2004

James C Housel
JAMES HOUSEL 2/23/04
SUPERVISORY PATENT EXAMINER
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